Functional MRI Correlates of Cognitive-Motor Learning

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Our knowledge of the supporting neural systems involved in cognitive-motor learning in humans is incomplete. Animal studies have suggested that the cerebellum, supplementary motor area (SMA), and basal ganglia are critical structures in this form of learning. Previous PET studies have yielded inconsistent findings, perhaps due to methodological problems, i.e., not controlling for movement rate. The present study examined the cerebellar and SMA contributions to motor sequence learning using whole-brain functional MRI (FMRI).

Subjects and Activation Task.
Twenty healthy subjects, between the ages of 19 and 43 and strongly right-handed (Edinburgh Inventory), participated after giving informed consent. The cognitive-motor learning task consisted of an adaptation of the Nissen-Bullemer (1) four-choice serial reaction time (RT) task. Subjects executed right index finger keypresses in response to a visual stimulus projected on a back-illuminated screen located at the subjects' feet. Stimulus was a filled box appearing within one of four open boxes, arranged in diamond formation. Subjects responded by pressing one of four keys on a keypad. Stimulus appeared for 900 msec; 100 msec intervened before next stimulus; keypress rate = 1 Hz. RT was measured from onset of stimulus to keypress. Each activation period consisted of 12 reaction time trials; an imaging series (block) consisted of 120 RT trials. Half of the subjects (n=10) received 5 blocks of trials that contained repetitions of a 12-element sequence. This was followed by one block of pseudorandom trials (Block 6). Blocks 7-10 consisted of the same repeated sequence of stimulus presentations as in Blocks 1-5. Subjects were not told of a repeating sequence before or during scanning, but were debriefed after Block 10. The remaining subjects (n=10) received 10 blocks consisting of pseudorandom stimulus presentations. This condition controlled for learning associated with perceptual-motor translation processes. Learning was defined by the behavioral dependent measure, i.e., mean reaction time per block.

FMRI Imaging Methods.
FMRI was conducted on a 1.5T GE Signa scanner equipped with a 30.5 cm i.d. 3-axis local gradient coil and an endcapped quadrature birdcage RF coil, using a blipped gradient-echo echo-planar pulse sequence (TE=40 ms; FOV=24 cm; 64 x 64 matrix; 3.75 mm resolution). Sixteen contiguous saggital slices (7 mm slice thickness) covering the entire brain were collected with a TR=4 s, with 64 consecutive images in each imaging series (block), yielding 10 alternating rest and activation periods of 12 s each. Functional data were converted to stereotaxic space (2), averaged across subjects within a group, and subtracted between groups for each of the 10 imaging runs.

Results.
Motor sequence learning occurred primarily during Blocks 1-5, as demonstrated by improved RT's in the Repeated Sequence group. The lateral cerebellum (left > right side) demonstrated significantly ($p<.001$) increased functional activity during the early stages of motor sequence learning (Blocks 1-5). The increased functional activity was not observed on Block 6 (Random condition), but re-emerged to a lesser extent after the sequence was over-learned (Repeated condition, Blocks 7-10). A similar pattern of learning effects, albeit smaller, were observed in the SMA. The Random Sequence group did not exhibit learning effects in RT or in functional imaging patterns.

Conclusions.
These findings indicate that the lateral cerebellum and, to a lesser degree, the SMA are critical in supporting the early stages of cognitive-motor sequence learning. This effect could not be explained by improved movement rates, since this variable was controlled. Of particular note, learning was observed primarily in the *left* lateral cerebellum (*contralateral* to the side of movement), suggesting that the effect was not related to primary motor execution.

References.
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